1632

PTO/SB/21 (03-03)
Approved for use through 04/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/904,181
Filing Date	July 11, 2001
First Named Inventor	Michael W. LEVITEN
Art Unit	1632
Examiner Name	Peter Paras, Jr.
Attorney Docket Number	R-456

Total Number of Pages in This Submission

ENCLOSURES (*Check all that apply*)

- ☑ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☑ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☑ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
- ☐ After Allowance Communication to a Technology Center (TC)
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual	Kelly L. Quast, Reg. No. 52,141
Signature	Kelly L Quast
Date	July 7, 2003

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: July 7, 2003

Typed or printed	Don Mixon		
Signature	Don Mix	Date	July 7, 2003

PTO/SB/17 (05-03)
Approved for use through 04/30/2003. OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 55.00

Complete if Known	
Application Number	09/904,181
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METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 50-1271

Deposit Account Name: Deltagen, Inc.

The Director is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☐ Credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater, For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	55.00
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 55.00

SUBMITTED BY

(Complete *(if applicable)*)

Name *(Print/Type)*	Kelly L. Quast	Registration No. *(Attorney/Agent)*	52,141	Telephone	650-569-5100
Signature	Kelly L Quast			Date	July 7, 2003

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/904,181	07/11/2001	Michael W. Leviten	R-456	1164

7590 03/07/2003

DELTAGEN, INC.
1003 Hamilton Avenue
Menlo Park, CA 94025

EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 03/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

RESP DUE 7-JUNE-03

Office Action Summary

Application No.	Applicant(s)
09/904,181	LEVITEN, MICHAEL W.
Examiner	**Art Unit**
Peter Paras, Jr.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,11,13-16 and 21-40* is/are pending in the application.

4a) Of the above claim(s) *1-4,11,13-16 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Applicant's amendment received on 12/18/02 has been entered. Claims 5-10, 12 and 17-20 have been cancelled. New claims 26-40 have been added. Claims 1-4, 11, 13-16, and 21-40 are pending. Claims 26-40 are under current consideration.

Election/Restrictions

Claims 1-4, 11, 13-16 and 21-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Priority

Applicants have amended the first line of the specification to include the serial number of the provisional application filed on June 26, 2001. Applicant's priority claim has now been perfected.

Sequence Compliance

Figure 2 contains an unidentified sequence. It appears that the sequence in Figure 2 is the nucleotide sequence of SEQ ID NO: 1 and that the omission of a sequence identifier number for said sequence is inadvertent. Since it appears that sequence listings in both paper and computer readable forms, which contain the nucleotide sequence of SEQ ID NO: 1, have been received and entered it is not

necessary to resubmit any sequence listings. However, in order to comply with the sequence rules (see 37 C.F.R. 1.821-1.825) the sequence in Figure 2 must be identified.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action, which fails to meet all of these requirements, will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

The following are new grounds of rejection under 35 USC § 101:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The claims are directed to a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits increased prepulse inhibition. The claims are further directed to cells isolated from the same mouse and method of screening agents that may modulate or ameliorate increased prepulse inhibition using the same mouse.

The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a ubiquitin-specific protease. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype related to a ubiquitin-specific protease. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ IN NO: 1. See the paragraph bridging pages 17-18.

The instant specification has disclosed a transgenic mouse whose genome comprises a disruption in SEQ ID NO: 1, wherein the mouse exhibits increased prepulse inhibition. See pages 48-49. The claims embrace such a mouse, cell obtained from the mouse and methods of identifying agents that affect prepulse inhibition in the same mouse. The instant specification has discussed that a phenotype of increased prepulse inhibition is the opposite of the prepulse response observed in schizophrenia patients. See page 49. However, the evidence of record does not provide a correlation between increased prepulse inhibition and any disease or disorder. Moreover, while the specification has purported that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a ubiquitin-specific protease (see page 6), the evidence of record has failed to provide a correlation between any ubiquitin-specific protease related disease/disorder and increased prepulse inhibition. The specification has provided general assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice.

As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be credible. The asserted utility does not appear credible to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between any ubiquitin-specific protease, increased prepulse inhibition, and any disease or disorder. Since the evidence of record has not provided a correlation between increased prepulse inhibition and any disease or disorder, the utility of identifying agents that affect increased prepulse inhibition is not apparent. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and credible.

The asserted utility of the transgenic mouse embraced by the claims is based on the expectation that disrupting the nucleotide sequence set forth in SEQ ID NO: 1 would result in a detectable phenotype in the mouse. The phenotype observed in the transgenic mice embraced by the claims is increased prepulse inhibition, which the instant specification has reported to be the opposite of would be observed in schizophrenia patients (schizophrenia patients have impaired prepulse inhibition). While impaired prepulse inhibition is suggested to be associated with schizophrenia, the association of increased prepulse inhibition with any disease has yet to be elucidated. Paylor et al (Psycopharmacology, 1997, 132 :169-180) contrast the startle responses of thirteen inbred mouse strains to investigate the potential genetic basis for differences in sensorimotor gating using the prepulse inhibition paradigm. It was found that some

certain strains showed high levels of prepulse inhibition while other strains showed low levels of prepulse inhibition. Paylor et al go on to discuss that impaired prepulse inhibition is associated with schizophrenia, obsessive-compulsive behavior and Huntington's disease and that rats exhibiting impaired prepulse inhibition can be used for screening potential new antipsychotic agents. See page 160. Paylor et al however does not discuss how increased prepulse inhibition relates to a disease or disorder.

Therefore, the reference suggests a need to provide independent evidence of an association of increased prepulse inhibition with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between increased prepulse inhibition and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be credible.

The following are new grounds of rejection under 35 USC § 112, 1st paragraph:

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

If the above enablement rejection regarding how to use the claimed transgenic mouse is overcome Applicants must also overcome the following scope of enablement issue regarding the nucleotide sequences embraced by the claims as set forth below:

Newly added claims 26-40 encompass a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits a phenotype of increased prepulse inhibition. The specification has disclosed mice and cells that comprise a disruption in the nucleotide sequence set forth in SEQ ID NO: 1. The specification has asserted that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a ubiquitin-specific protease. The state of the art however suggests that the family of ubiquitin-specific proteases comprises many members that have different structures and functions (i.e. they act on different substrates). See Finley et al [1991, Annual Review of Cell Biology, Ubiquitination, pages 25-69, provided in Applicant's IDS] who discuss the structures and functions of various enzymes of the ubiquitin system across species. Also see the instant specification (on page 1, in lines 12-19), which reports on the diversity of the ubiquitin-specific protease family. Moreover, the claims as written are very broad with regard to

target genes (even broader than genes encoding ubiquitin specific proteases) as they now encompass target genes that can recombine with a nucleotide sequence homologous to SEQ ID NO: 1. As such the claims broadly encompass disruption of nucleotide sequences encoding proteins, which have different structures and functions. The term homologous can be broadly interpreted to read on nucleotide sequences that share homology of a single nucleotide base. Such an interpretation of the definition of homology allows for any target sequence to be encompassed by the claims because all four nucleotide bases are contained within the nucleotide sequence set forth in SEQ ID NO: 1. The evidence of record fails to provide guidance or working examples that correlate disruption of any target sequence with a phenotype of increased prepulse inhibition in a transgenic mouse. Moreover, given the breadth of the claims directed to any target sequence the skilled artisan would not be able to predict if disruption of any target sequence would result in a phenotype of increased prepulse inhibition. The state of the art suggests that one of skill could not predict the phenotype of a knockout mouse (Moreadith et al., 1997, J. Mol. Med., Vol. 75, pages 208-216; see page 208, column 2, last full paragraph). Moens et al. (Development, Vol. 119, pages 485-499, 1993) disclose that two mutations produced by homologous recombination in two different locations of the N-myc gene produce two different phenotypes in mouse embryonic stem cells, one leaky and one null (see abstract). In light of these references, it is unpredictable if a disruption in any target gene would result in a phenotype of increased prepulse inhibition in a transgenic mouse. Furthermore, the target genes, other than the target gene comprising SEQ ID NO: 1, embraced by the claims, which when disrupted

result in a phenotype of prepulse inhibition in a transgenic mouse have not been disclosed. If there is no disclosure of starting material or of any conditions under which claimed process can be carried out, undue experimentation is required, and there is failure to meet enablement requirement that cannot be rectified by asserting that all disclosure related to process is within skill of art. See Genentech Inc. v. Novo Nordisk A/S 42 USPQ2d 1001, 1997. In this case the starting material that has not been disclosed is any other target gene capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1 which when disrupted results in a phenotype of increased prepulse inhibition in a transgenic mouse. Given the lack of guidance provided by the instant specification with regard to the other target genes embraced by the claims it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Limiting the claims to disruption of the nucleotide sequence set forth in SEQ ID NO: 1 may be sufficient to overcome this aspect of the rejection.

Applicant's arguments filed 12/16/02 have been fully considered but they are not persuasive. Applicants have presented new claims to more clearly define the target gene. Applicants submit that the newly added claims are fully enabled with regard to target genes.

In response, the Examiner asserts that the newly added claims actually have a broader scope with respect to the target gene than the originally filed claims. The claims now recite a target gene capable of homologous recombination with a nucleotide

sequence homologous to SEQ ID NO: 1. Since the claim requires that the nucleotide sequence, which recombines with the target gene, share homology with SEQ ID NO: 1 and since the degree of homology is unknown and could be reasonably interpreted to be as little as a single base or even a codon, the target gene could also be interpreted to read on any gene. The guidance and working examples provided by the specification fail to provide a correlation between disruption of any target gene, in a transgenic mouse, and a phenotype of increased prepulse inhibition. It is unpredictable is disruption of any target gene in a transgenic mouse would result in a phenotype of increased prepulse inhibition. See above. Thus, the instant specification has failed to enable the claims with respect to target genes.

New Matter

Claims 26-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The claims embrace a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits a phenotype of increased prepulse inhibition.

The specification provides no implicit or explicit support for the context of the disruption of a target gene that is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1. The specification has only provided support for disruption of a target gene that encodes a ubiquitin-specific protease that results in a phenotype of prepulse inhibition in a transgenic mouse. In particular the specification has provided support for disruption of a target gene that comprises the nucleotide sequence set forth in SEQ ID NO: 1 that results in a phenotype of increased prepulse inhibition in a transgenic mouse. Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often

necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure* [or point to case law supporting incorporation of such a limitation as in the instant case]".

Limiting the claims to disruption of the nucleotide sequence set forth in SEQ ID NO: 1 may be sufficient to overcome this rejection.

Claims 26-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits a phenotype of increased prepulse inhibition.

The specification has disclosed a transgenic mouse whose genome comprises a disruption in a target gene comprising the nucleotide sequence set forth in SEQ ID NO: 1, wherein the mouse exhibits a phenotype of increased prepulse inhibition. The specification however has not disclosed the other target genes, embraced by the claims, within the genus of target genes that are capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1 [The term homologous can be broadly interpreted to read on nucleotide sequences that share homology of a single

nucleotide base. Such an interpretation of the definition of homology allows for any target sequence to be encompassed by the claims because all four nucleotide bases are contained within the nucleotide sequence set forth in SEQ ID NO: 1].

Based upon the prior art there is expected to be sequence variation among the species of target genes embraced by the claims because the claims broadly embrace any target gene sequence. The specification discloses disruption of a target nucleotide sequence (SEQ ID NO: 1) that is purported to encode a ubiquitin protease and does not disclose other target nucleotide sequences. There is no evidence on the record of a relationship between the structure of the nucleotide sequence set forth in SEQ ID NO: 1 and the other target genes embraced by the claims that would provide any reliable information about the structure of other target genes within the genus. There is no evidence on the record that the nucleotide sequences set forth in SEQ ID NO: 1 had a known structural relationship to any other target gene sequences; the specification discloses only a target nucleotide sequence comprising the nucleotide sequence set forth in SEQ IN NO: 1; the art indicated that there is variation between gene sequences. There is no evidence of record that would indicate that any of the other target genes embraced by the claims, which when disrupted in a transgenic mouse result in a phenotype of increased prepulse inhibition. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus of target genes, because the nucleotide sequence set forth in SEQ ID NO: 1 is not representative of the claimed genus. Consequently, since Applicant was in possession of only the nucleotide

sequence set forth in SEQ ID NO: 1 and since the art recognized variation among the species of the genus of DNA target sequences, the nucleotide sequence set forth in SEQ ID NO: 1 was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of target genes as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Limiting the claims to disruption of the nucleotide sequence set forth in SEQ ID NO: 1 may be sufficient to overcome this rejection.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 5-7 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The previous rejection of claims 5-10 under 35 U.S.C. 103(a) as being unpatentable over Capecchi taken with Woods is withdrawn.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER